DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

M3579M

Food and Drug Administration
Rockville MD 20857

CBER-00-017

MAR 16 2000

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Mr. James A. Monsor
Director of Operations
ALK-Abello, Inc.
1700 Royston Lane
Round Rock, TX 78664

Dear Mr. Monsor:

The Food and Drug Administration (FDA) conducted an inspection of ALK-Abello, Inc., 1700 Royston Lane, Round Rock, Texas, between October 18-22,1999. During the inspection, our inspectors documented significant deviations from the applicable standards and requirements of Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), and Title 21, Code of Federal Regulations, (21 CFR), Parts 211, and 600-680 as follows:

1. Failure to establish, maintain, and follow adequate written procedures describing the handling of all written and oral complaints regarding a drug product including the need for an investigation in accordance with §211.192 [21CFR 211.198(a)] in that:

   a. Investigations into five complaints regarding discolored products and seven complaints regarding excessive precipitates were not always completed and impact on product was not always assessed.

   b. Complaints received by headquarters in Wallingford, CT were not always forwarded in a timely manner to the manufacturing facility at Round Rock, TX for investigation and follow-up.

2. Failure to establish and follow written procedures for the surveillance, receipt, evaluation, and reporting of adverse experiences to FDA [21CFR 600.80(b)] in that product complaints involving Tree Mix lot 8T21F27824, Treatment set lot 73009-4, and Johnson

Grass lot 7X63F23 Treatment set, were not always assessed for compliance with FDA adverse event reporting requirements.

3. Failure to ensure that reprocessed batches will conform with all established standards, specifications, and characteristics [21CFR 211.115(a)] in that there was no written procedure and validation data that supports the [redacted] of bulk product following a failed sterility test without an assignable cause for the contamination.

4. Failure to assure that container closure systems are not reactive, additive, or absorptive so as to alter the safety, identity, strength, quality, or purity of the drug product and to provide adequate protection against factors in storage and use that can cause deterioration or contamination of the drug product [21CFR 211.94] in that container closure system integrity and compatibility studies have not been performed.

5. Failure to establish scientifically sound and appropriate specifications, standards, sampling plans, and test procedures designed to assure that drug products conform to appropriate standards of identity, strength, quality, and purity [21 CFR 211.160(b)] in that preservative effectiveness tests have not been performed for all filled products.

6. Failure to establish separate or defined areas or other control systems for manufacturing and processing operations to prevent contamination or mix-up [21CFR 211.42(c)(10)(iv)] in that surface environmental monitoring was not performed in the [redacted] hoods where aseptic filling occurs

7. Failure to establish and follow written testing programs designed to assess the stability characteristics of drug products [21CFR 211.166] in that not all tests ([redacted]) were consistently performed at the established test intervals for standardized allergenic extracts.

We acknowledge receipt of your response dated November 5, 1999, to the Form FDA 483 issued at the close of the inspection and the updates provided during the January 31, 2000, conference call meeting between FDA and ALK-Abello representatives. Corrective actions addressed in your letter may be referenced in your response to this letter, as appropriate. Our evaluation of your response follows, and is numbered to correspond to the items listed on the Form FDA 483:

2a-f. Please clarify whether notification to the agency will be done regarding the adverse experience reporting.

6/19. The response indicated that reprocessing would not be performed for any product that fails sterility testing. Please note that if reprocessing is performed in the future, the reprocessing procedures must be validated and submitted as a prior approval supplement to your license

7/13. The response indicated that all failures including sterility and environmental outages will be more thoroughly investigated and documented. Please note that the details of the investigation depend on the type and processing of the product manufactured

Investigations should at least include review of area maintenance documentation, sanitization documentation, physical and operational parameters and training status of personnel involved. In addition, please note that identifying the isolates recovered from monitoring methods may be useful when identifying the source of microbial contamination in a product or process.

Neither this letter nor the list of inspectional observations (Form FDA 483) is meant to be an all-inclusive list of deviations. It is your responsibility to ensure that your facility is in compliance with the provisions of the Federal Food, Drug, and Cosmetic Act and all applicable regulations. You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action without further notice. Such actions include seizure, injunction, license suspension and/or revocation. Federal agencies are advised of the issuance of all Warning Letters about drugs so that they may take this information into account when considering the award of contracts.

You should notify this office in writing, within 15 working days of receipt of this letter, of any additional specific steps you have taken to correct the noted deviations and to prevent their recurrence. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed.

Your reply should be sent to the following address: Mr. Steven A. Masiello, Director, Office of Compliance and Biologics Quality, Center for Biologics Evaluation and Research, Attention: Division of Case Management, HFM-610, 1401 Rockville Pike, Suite 200N, Rockville, MD 20852-1448.

Sincerely,

Deborah D. Ralston

Deborah D. Ralston
Director
Office of Regional Operations